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TITLE: "Integrated Genomic Biomarkers to Identify Aggressive Disease in African Americans with Prostate Cancer"

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CONTRACTING ORGANIZATION: Henry Ford Health System
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of our research is to identify somatic copy number alterations and methylation markers in the primary tumors of African American (AA) men that can serve as a component of their recurrence risk assessment and be applied in treatment planning in attempt to reduce the racially disparate rates of mortality from prostate cancer. Through whole genome copy number alteration and methylation scans, the study will identify individual and integrated DNA-based biomarkers of biochemical recurrence in 200 AA men (100 with and 100 without biochemical recurrence). These biomarkers will then be validated in an independent set of 200 AA men. In the first year of funding, we have enumerated both discovery and validation samples; have obtained formalin fixed paraffin embedded blocks from 300 of these men; have completed pathology review of the complete discovery sample tumors; macrodissected and performed DNA extraction from 141 tumors; completed the running and quality control of 60 tumors on the copy number assay; completed the running and quality control of 48 tumors on the Illumina EPIC methylation microarrays. From the resulting copy number and methylation data, we have preliminary results for Aim 1 suggesting the utility of using the GEMCaP for prediction of biochemical recurrence in AA men, and further encouraging findings that suggest many, but not all, previously identified CpG methylation sites associated with biochemical recurrence in European American men are also associated with risk of recurrence in AA men. In addition, we also present finding from The Cancer Genome Atlas on copy number alterations that differ by race-ethnicity in AA vs. EA men with prostate cancer and are consistent with race-ethnicity differences observed in breast cancer. We intend to test these cross tumor site race-differentiated copy number alterations with biochemical recurrence in our study following completion of the discovery cohort. We are also expand the sample size for our manuscript exploring the effectiveness of a commonly used clinicopathologic predictor of prostate cancer in AA men and whether that effectiveness depends on genetic African ancestry, which is significant as we proposed that our genomic biomarkers would add to this established predictor.

15. SUBJECT TERMS

prostate cancer; DNA; copy number alterations; methylation; biomarker; racial disparities; integrative.

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1. INTRODUCTION:

Approximately ~33,000 men die each year from prostate cancer (CaP), in particular from disease recurrence. African American men have higher CaP mortality rates than age matched European American males. Risk of disease recurrence after primary treatment is difficult to predict with clinical variables and prostate specific antigen. Robust methods for risk stratification of prostate tumors are needed to enable men and their physicians to safely select between post-treatment surveillance and immediate adjuvant therapy. The purpose of our research is to use a mulit-omic approach to identify somatic copy number alterations and methylation markers in the primary tumors of African American men that can serve as a component of their recurrence risk assessment and be applied in treatment planning to help reduce the racially disparate rates of mortality from CaP. Through whole genome copy number alteration and methylation scans, the study will identify individual and integrated DNA-based biomarkers of biochemical recurrence in 200 African American men (100 with and 100 without biochemical recurrence). These biomarkers will then be validated in an independent set of 200 African American men.

2. KEYWORDS:

prostate cancer; DNA; copy number alterations; methylation; biomarker; racial disparities; integrative.

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**

Major Task #1: Identify subjects and tissue specimens for biomarker discovery and validation.

- Identify from the existing database at Henry Ford Health System (HFHS) lists of eligible prostatectomy patients as defined in the Research Strategy, confirm availability of banked formalin fixed and paraffin-embedded (FFPE) prostate tissue with biorepositories. Target completion January 31st 2016; Completed January 1st 2016

- Calculate CAPRA-S scores for all eligible subjects. Target completion January 31st 2016; Completed January 15th 2016

- Perform incidence sampling to determine discovery and validation study samples. Target completion September 1st 2016; Discovery sample 100% completed September 1st 2017

- Tumor blocks will be pulled from archive, determination of the optimal block, and sections cut and tumor areas marked by pathologist. Target completion September 1st 2017; Discovery sample pathologic review completed September 1st 2017

- Pathology review of cut cases and slides transferred to UCSF. Target completion January 1st 2018; Discovery sample 70% completed as of September 1st 2017

Major Task #2: Tissue processing and DNA extraction for entire project.

- Manual tumor tissue macrodissection. Target completion January 1st 2018; Discovery sample 70% completed as of September 1st 2017

- DNA extraction and quality assessment. Target completion February 28th 2018; Discovery sample 70% completed as of September 1st 2017

Major Task #3: Perform genomic microarray experiments.

- Carry out array comparative genomic hybridization (aCGH) on Aim 1 DNAs at UCSF. Target completion date September 1st 2017; Agilent reagent quotes obtained. Reagents ordered. 60 samples run and passed QC as of September 1st 2017. We have specifically put this on hold to see if we can derive both methylation and copy number alterations from the Illumina EPIC arrays.

- Quality control for aCGH and determination of copy number via CBS. Target completion date September 1st 2017; 60 samples run and passed QC as of September 1st 2017.

- Quality control of methylation microarray data and preparation of an analysis dataset. Target completion date September 1st 2017; An initial analysis set of 48 samples has been compiled, QCed and initial analyses have been completed (see next section) as of September 1st 2017.

- Conduct methylation microarray experiments on Aim 1 DNAs. Target completion date September 1st 2017; Worked out an agreement with Illumina to provide methylation reagents for 1st 48 samples to determine if the Illumina EPIC arrays are going to be useful in also identifying copy number alterations in FFPE preserved prostate tumors from African Americans. Reagents ordered. Established agreement with a core at USC for array processing. A pilot data set of 48 samples with both Agilent aCGH and Illumina EPIC methylation array data was finalized on August 22nd, 2017. We doing methods work and are currently assessing the agreement between the copy number calls from the aCGH arrays and those obtained from the EPIC methylation array to determine if both need to be used for the study or if we can use the EPIC array to do both (see preliminary findings in next section)

Major Task #4: Statistical analyses for GEMCaP and published methylation biomarkers. Target completion November 1st 2017; Based on our initial discovery sample set, preliminary analyses for GEMCAP and single CpG sites have been conducted as of September 21st 2017.

Major Task #5: Discovery of African American specific copy number and methylation biomarkers. Target completion Febuary 1st 2018; not yet started.

Major Task #6: Validate integrated biomarker panel in a separate discovery set of African American prostate cancer. Target completion July 1st 2018; not yet started.

Major Task #7: Draft manuscripts for publication.

Manuscript #1: CAPRA-S performance in an African American population. 50% completed as of September 1st 2017.

Manuscript #2: Prostate and breast cancers harbor common somatic copy number alterations that consistently differ by race-ethnicity. Target completion November 2017; 90% completed as of September 1st 2017.

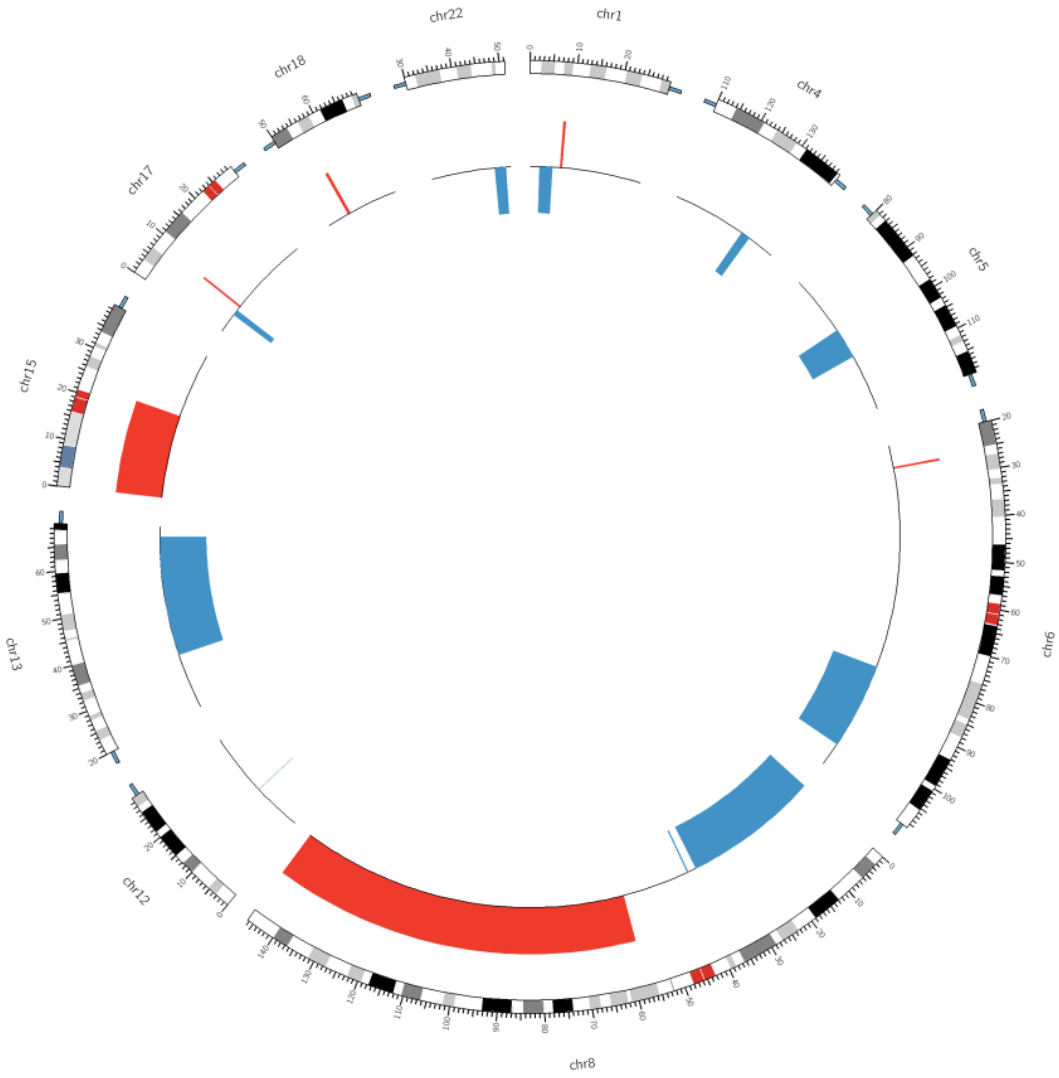
What was accomplished under these goals?

In the current reporting period, our major activities were the identification of the study subjects, abstraction of their clinical and pathologic data, acquisition of their FFPE tumor tissue blocks, pathologic review of each case, sectioning of blocks, DNA extraction, genomic analysis (aCGH and methylation) and preliminary analyses for Aim 1 (the evaluation of existing DNA alteration-based by markers of biochemical recurrence in African Americans). To date, we have identified all 200 subjects for the discovery cohort, and their tissue blocks have been acquired. Of those, 200 (100%) have undergone pathologic review. Among these subjects, 141 have been sectioned and have undergone DNA extraction. For the 200 validation cohort subjects, we have identified all 200 subjects (100%) of the subjects, and we are currently in the process of obtaining the corresponding FFPE blocks. Of the 200 validation subjects, we have currently retrieved FFPE blocks for 79 of the subjects. We will proceed with the pathologic review, sectioning, and DNA extraction for the validation study subjects.

For Aim 1 and the evaluation of existing DNA-based biomarkers of recurrence, multiple preliminary analyses have been conducted. Based on the 60 Agilent aCGH arrays successfully run, we have compared two methods for somatic copy number alteration detection, Circular Binary Segmentation (CBS) and the Agilent Aberration Detection Method 2 (ADM-2). The agreement between the two algorithms was approximately 86% across the tumor samples, providing confidence that a clear majority of regions identified are not dependent on a single copy number alteration detection method. The ADM-2 algorithm employs a Hidden Markov model, and in our experience, it is a more sensitive method than CBS. As a result, we will use the results from the ADM-2 algorithm going forward, while using CBS as a quality check on the primary analysis.

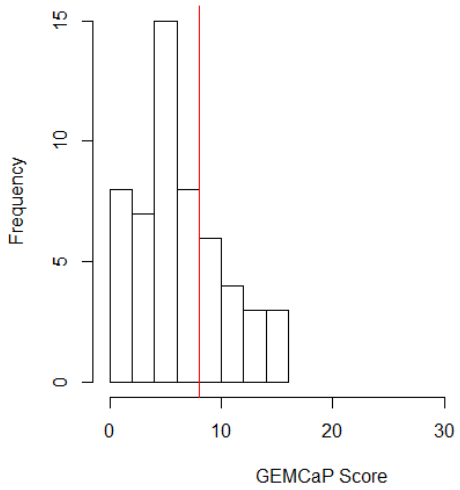
Using Gistic2 (with a false discovery rate threshold of 0.1) on the ADM-2 aCGH segmentation results, we identified 10 statistically significant regions of frequent deletion and 6 statistically significant regions of frequent amplification in these tumors. These copy number alterations are displayed in Figure 1, with deletions displayed in blue and amplification displayed in red. Among these alterations, these findings show the prostate cancer characteristic copy number loss on chromosome 8p and gain on 8q.

Figure 1: Circos plot of significant regions of copy number deletion (blue) and amplification (red) in the 60 African American discovery subjects.



Further, ADM-2 derived copy number alterations were used to determine the GEMCaP biomarker status for each tumor. To achieve this, the 38 copy number alteration regions (15 gain and 23 loss) that make up the GEMCaP biomarker were scored for each tumor, and these component scores were then summed to produce the GEMCaP score with values from 0 to 38. The distribution on these scores in our study is shown in Figure 2. The maximum GEMCaP score value observed was 16. For each unit increase in the GEMCaP score, we observed an increase in the risk of biochemical recurrence of 1.2-fold (95%CI 1.00-1.44; p=0.055).

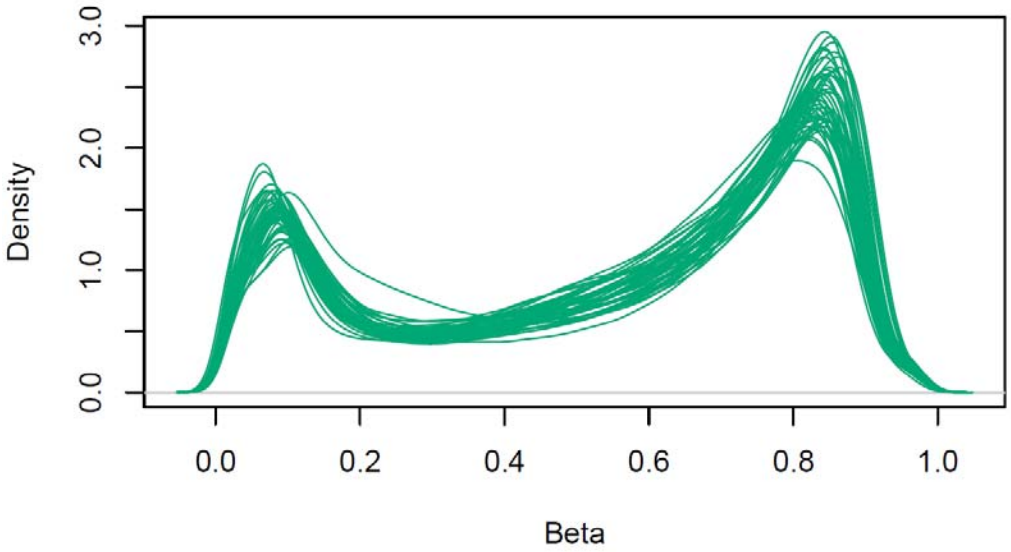
Figure 2: Histogram of the GEMCaP scores observed. The red vertical line is drawn at a GEMCaP score of 8 (i.e. the GEMCaP biomarker positive threshold as determined in European Americans)



The threshold used to determine GEMCaP biomarker positivity was a score ≥ 8 (i.e. >20% of the component alterations positive), a threshold established in the original GEMCaP publication. Based on this threshold, 43% of the subjects were GEMCaP positive, which was substantially higher than our original estimate of 7% in an independent sample of 28 African Americans with prostate cancer and above our estimate of 33% in the European American men it that study (Levin et al. Cancer Epidemiology Biomarkers and Prevention 2014). Those who were biomarker positive had a 2.61-fold (95%CI 0.49-13.87; p=0.261) increased risk of developing a biochemical recurrence. This increased risk associated with GEMCaP biomarker positivity in African Americans is consistent with our published data from an independent study. While this effect has not achieved statistical significance, this preliminary result is encouraging, as it only represents ~30% of the total discovery cohort.

Additionally, the newest Illumina methylation arrays, EPIC, were pilot tested on a subset of 48 subjects (24 with biochemical recurrence and 24 who were biochemical recurrence free at last follow-up) from those 60 with aCGH copy number. After quality assessment of the individual CpG sites on the array, 748,142 were deemed to be of sufficient quality for subsequent analysis. The distribution of the methylation beta-values for each of the 48 tumors profiled are presented in Figure 3. These distributions show the characteristic peaks near a value of zero (unmethylated) and one (completely methylated), as well as the compression of the signals at each of these extreme values which we expected to see from FFPE samples. The distributions appear consistent across tumors, with no obvious outliers present in the data. As a result, all 48 samples were retained for further analyses.

Figure 3: Density plot of CpG site specific methylation beta values for 748,142 for each of the 48 tumors profiled using the Illumina EPIC array.



We next performed a preliminary analysis of a previously published set of biochemical recurrence associated CpG sites in 25 genes from a study by Mahapatra et al (Clinical Cancer Research 2012). This published study consisted of European Americans only, and all 25 CpG sites were hypermethylated in biochemically recurrent prostate cancer relative to those without biochemical recurrence. In analyses from our cohort of African American men, we observed statistically significant ($p<0.05$) hypermethylation in 68% (17 out of the 25) of the genes in biochemically recurrent in comparison to non-biochemically recurrent cases. Again, while still preliminary, these consistent cross-ethnic results are encouraging given that the sample set included less than 25% of the total discovery cohort. Further, these findings also suggest that the identification of ethnic specific markers will also be fruitful.

In addition to generating preliminary results for Aim 1, we conducted this pilot study of 48 subjects with parallel measurement of copy number and methylation alteration to evaluate the effectiveness of the EPIC methylation array data to be used to also call copy number alterations. Multiple methods have been developed to call somatic copy number alterations using the Illumina methylation arrays (prior to the Illumina Epic release), with accuracy dependent upon tissue preservation and tumor type. Feber et al. (Genome Biology 2014) developed the most established method, which is now implemented in the methylation bioinformatics pipeline called the Chip Analysis Methylation Pipeline (ChAMP). In their manuscript describing this method, they analyzed data from multiple tumor types and in both FFPE and fresh frozen tissue from The Cancer Genome Atlas (TCGA). FFPE-based results produced lower accuracy, and of the tumor sites studied, the method had the lowest accuracy in prostate tumors. Using the ChAMP

algorithm run in case-only mode (we do not yet have a normal tissue comparison), we evaluated its ability to capture the 2,183 copy number alterations identified by aCGH in our pilot data from 48 African American subjects. The range of the per tumor proportion of aCGH array identified copy number alterations also identified by ChAMP was 0%-86%, with a mean of 29%. There was no obvious trend in these proportions with the number of alterations in each tumor or time since preservation. One clear difference with prior studies is the lack of a normal comparison tissue. We are currently trying to obtain a set of appropriate normal, FFPE prostate tissue with EPIC methylation data to attempt to boost these capture rates, as well as testing the performance of other methods, but based solely on the current analyses, the data suggest that we will not be able to use the EPIC platform for accurate copy number alteration in our study.

As one of our objectives is to develop somatic DNA-based biomarkers that augment the ability of current clincopathologic tools (e.g. CAPRA-S) to predict recurrent disease in African Americans, and given that the performance of these clinicopathologic predictors in African American men have not been well described in the literature, we performed an analysis comparing the effectiveness of the Cancer of the Prostate Risk Assessment Post-Surgical (CAPRA-S) score at predicting biochemical recurrence in African American and European American men. Our findings suggested that CAPRA-S performed similarly in both self-identified race-ethnicities. As African Americans are an admixed population, with ancestry derived from both Africa and Europe, we also asked the question if the effectiveness of CAPRA-S differed by the percentage of African ancestry in African American men. Our findings suggest no differences in the predictive ability of CAPRA-S based on percent genome-wide African ancestry. We presented these initial findings at the CDMRP 2016 Innovative Minds in Prostate Cancer Today meeting. Our results show that it is valid to adjust for CAPRA-S in our analytic strategy to identify genomic alterations that add to this clinicopathologic predictor of BCR, leading to further improvements in clinical recurrence risk prediction in African Americanmen and more refined identification of those likely to benefit from earlier adjuvant therapy. We have expanded the sample size for this analysis, which has taken additional time and effort to perform the chart abstraction, and plan to publish these findings in the next reporting period. The sample size now includes approximately 1,000 African American men that make up the cohort from which the discovery and validation samples have been drawn for this study, as well a matched set 1,000 European American men. While the results are similar to the smaller set, this larger sample size allows us make a more definitive statement about the cross-ethnic applicability of this prognostic pathologic marker of recurrence risk.

Finally, as the objective of this proposal is to identify DNA-based alterations that may act as optimal prognostic markers of biochemical recurrence in African American men, we performed a parallel analysis of the copy number alteration data present in TCGA to identify such alterations that differ by race-ethnicity that may help guide our analysis. In the 267 European American TCGA prostate tumors, Gistic2 identified 43 copy number alterations. Of these, 17 (39.5%, total 182.8 Mb in length) were amplifications and 26 (60.5%, total 457.7 Mb in length) were deletions. In the 42 African American TCGA prostate tumors, 22 copy number alterations were

identified. Of these, 2 (9.1%, spanning 0.11 Mb) were amplifications, and 20 (90.9%, spanning 30.1 Mb) were deletions. These copy number alterations were pooled, resulting in 74 prostate cancer copy number alteration.

Of these 74, 21 (28% of 74; 5 amplifications and 16 deletions) significantly differed by race-ethnicity. In addition, African American prostate tumors contained more extreme copy number alterations at both regions of amplification (80%, 4 of 5) and deletion (81%, 13 of 16). We used data from our previously publishedprostate tumor dataset (Cheng et al Genes, Chromosomes, and Cancer 2012) containing 31 European Americans and 29 African Americans to validate the observed race-ethnicity copy number magnitude differences in the 21 race-differntiated alterations identified in the TCGA prostate discovery data. In this dataset, copy number alterations were profiled using the Illumina 1M genome-wide single nucleotide polymorphism genotyping. Overall, 14 of the 21 (66.7%) race-differentiated copy number alterations showed consistent effects when compared with the TCGA discovery. This included 13 of the 16 (81.3%) deletion regions. Suggestive significant race-differentiated effects were attained for one deletion on chromosome 11 (p-value = 0.082) and one deletion on chromosome 5 (p-value=0.106), where both of these copy number alterations showed more extreme loss in African American relative to European American prostate tumors.

We also used a cross-tumor approach by attempting to validate these alterations that differ by race-ethnicity in the TCGA breast tumors. We chose breast cancer because, similar to prostate cancer, it is also a hormonally driven cancer. A total of nine (42%, 9 of 21) race-differentiated copy number alterations identified in TCGA prostate tumors overlapped with race-differentiated breast cancer copy number alterations. These nine copy number alterations reside on chromosomes 5, 6, 8, 11, 13, and 16. In both tumor types, the chromosome 8q alterations were the sole amplifications and the remaining were deletions. For 6 of the 9 (67%) overlapping copy number alterations, African American prostate and breast tumors both had more extreme alterations. These included two amplification on chromosome 8 and four deletions on chromosome 5, 11, and 13.

We have completed a draft manuscript detailing our race-differentiated obserations across tumor types using public datasets, and are currently revising it for submission by November 2017. Our target journal is Cancer Research. Also, in the full discovery sample, we will evaluate the association between these race-differentiated copy number alterations and biochemical recurrence.

- **What opportunities for training and professional development has the project provided?**

  Dr. Paris at UCSF had a summer intern this past summer who was part of the UCSF Minority Training Program in Cancer Research. This DoD project allowed the student to gain experience in pathology review, macrodissection and DNA extraction. She also participated in monthly UCSF-Henry Ford team meetings.

- **How were the results disseminated to communities of interest?**

Nothing to report

- **What do you plan to do during the next reporting period to accomplish the goals?**

1. Complete the pathologic review of all 400 tumors; sections for all tumors will be cut and sent to UCSF for macrodissection, DNA extraction, and if needed, copy number array profiling.
2. Complete a methods manuscript describing the results from a pilot study of 48 tumors (24 with and 24 without biochemical recurrence that are part of the discovery sample) to determine the sensitivity and specificity of the new Illumina EPIC methylation arrays to recover copy number alterations in the tumors, as this has not been reported to date.
3. Conduct all methylation array experiments for the discovery sample.
4. Complete manuscript on the performance of CAPRA-S in African American men and whether its effectiveness differs by genome-wide percent African ancestry.
5. Complete manuscript on the identification of race-differentiated copy number alterations in prostate and breast tumors.

4. IMPACT:

a. **What was the impact on the development of the principal discipline(s) of the project?**

Our initial findings from genome-wide copy number and methylation data suggest that some molecular biomarkers of biochemical recurrence discovered in European American will apply to African American men. However, differences are also apparent and justify discovery of ethnic specific markers African American men.

Our finding of similar effectiveness of CAPRA-S in African American men in comparison to European American men is something that is not established in the literature. These results impact clinical care of African American men with prostate cancer as they establish that CAPRA-S can be used effectively in assessing risk of recurrence in this minority population that suffers disproportionately from prostate cancer.

Our TCGA-based findings have identified race-differentiated copy number alterations in prostate cancer that are consistently race-differentiated in breast cancer, another hormonally driven tumor type.

b. **What was the impact on other disciplines?**

Our manuscript using TCGA data that details the race-differentiated copy number alterations that are unique and shared between prostate and breast has an clear impact on the field of breast cancer racial disparities.

In this same manuscript, we developed a new area under the curve method for quantifying copy number alterations and testing with outcomes. This new approach could be used in the analysis of copy number alterations in any tumor type and therefore has impact on cancer research in general.

What was the impact on technology transfer?

Nothing to report

c. **What was the impact on society beyond science and technology?**

Nothing to report

6. CHANGES / PROBLEMS:

a. **Changes in approach and reasons for change**

We have made the decision to not match our biochemical recurrence and non-recurrence subjects on CAPRA-S score as part of the design. Rather, we will adjust for CAPRA-S as part of our analysis to ensure that our biomarker(s) provide added value to CAPRA-S.

b. **Actual or anticipated problems or delays and actions or plans to resolve them**

The delay for this reporting period is similar to the last. While we have increased our pace, FFPE block retrieval and pathologic review remained a bottleneck. We have worked closely with our colleagues in pathology to solve both issues, this includes our pathologist (Dr. Nilesh Gupta), and we have identified a research pathologist (Dr. Kanika Teneja), who does not have clinical responsibilities. With Dr. Teneja's help over the last two months, Dr. Gupta has been able to complete the review of the discovery cohort. With this collaborative pathology effort in place, we believe that we will be able to realistically complete the review of all 400 tumors by the April 2018.

c. **Changes that had a significant impact on expenditures**

Nothing to report

d. **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

e. **Significant changes in use or care of human subjects**

Nothing to report

f. **Significant changes in use or care of vertebrate animals.**

Nothing to report

g. **Significant changes in use of biohazards and/or select agents**

Nothing to report

7. PRODUCTS:

a. **Publications, conference papers, and presentations**

Presentation #1 DoD IMPaCT Meeting 2016, Bethesda, MD: "The impact of self-identified race-ethnicity and genetic ancestry on a commonly used clinicopathologic predictor of biochemically recurrent prostate cancer".

i. **Journal publications.**

Nothing to report

ii. **other non-periodical, one-time publications.**

Nothing to report

iii. **Other publications, conference papers, and presentations.**

Nothing to report

b. **Website(s) or other Internet site(s)**

Nothing to report

c. **Technologies or techniques**

Nothing to report

d. **Inventions, patent applications, and/or licenses**

Nothing to report

e. **Other Products**

Nothing to report

8. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

a. **What individuals have worked on the project?**

Name:	*Albert M. Levin, PhD*
Project Role:	*co-PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*Dr. Levin is the PI for the Henry Ford site. In addition to the design of the study, he is overseeing the process of tissue acquisition, pathology review, clinical/pathological data abstraction, histological staining and sectioning of the blocks, specimen shipment, data analysis, and manuscript writing.*
Funding Support:	*DoD; The Fund for Henry Ford*

Name:	*Pamela L. Paris, PhD*
Project Role:	*co-PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*Dr. Paris is the PI for the UCSF site, which is doing all of the DNA extractions and copy number array profiling. She is also working closely with Dr. Levin on oversight of pathologic review and tissue preparation, as well as development and writing of manuscripts based on the cohort.*
Funding Support:	*DoD*

Name:	*Benjamin A. Rybicki, PhD*
Project Role:	*co-I*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Rybicki has provided mentorship and guidance for all aspects of the study development for Dr. Levin. He also participates in the development and the writing of manuscripts for the study.*
Funding Support:	*DoD*

Name:	*Nilesh Gupta, MD*
Project Role:	*Pathologist*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Gupta is responsible for the pathologic review of all of the tumors from the cohort subjects.*
Funding Support:	*DoD; The Fund for Henry Ford*

Name:	*Kanika Teneja, MD*
Project Role:	*Research Pathologist*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Dr. Teneja is working with Dr. Gupta to increase the pace of review all of the tumors from the cohort subjects.*
Funding Support:	*The Fund for Henry Ford*

Name:	*Sudha Sadasivan, PhD, MPH*
Project Role:	*Study coordinator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*Dr. Sadasivan is responsible for the day-to-day management of all aspects of the project.*
Funding Support:	*DoD; The Fund for Henry Ford*

Name:	*Khanh Kieu, BA*
Project Role:	*Laboratory technician*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*5*
Contribution to Project:	*Mr. Kieu is responsible for the acquisition of the tumor blocks, abstraction from the original pathologic review to determine within which blocks the index nodule is located, and normal tissue macrodissection, and normal tissue DNA extraction.*
Funding Support:	*The Fund for Henry Ford*

Name:	*Lonia Martin, MSA*
Project Role:	*Grant Administrator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Ms. Martin is responsible for the she will oversee the financial operation relating to the data management for the project, monitoring all aspects and ensuring the correctness of expenses charged to the grant.*
Funding Support:	*The Fund for Henry Ford*

b. **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to report

c. **What other organizations were involved as partners?**

Nothing to report

9. SPECIAL REPORTING REQUIREMENTS

Not applicable

10. APPENDICES:

Nothing to report